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December 17, 2003

Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building (1101A)
1200 Pennsylvania Ave., NW
Washington, DC 20460

Re: Comments on the HPV test plan for Isooctadecanoic Acid reaction products with TEPA

Dear Administrator Leavitt:

The following are comments on the HPV test plan for Isooctadecanoic Acid reaction products with TEPA (CAS no. 68784-17-8), submitted by the American Chemistry Council (ACC). These comments are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health and environmental protection organizations have a combined membership of more than ten million Americans.

ACC submitted its test plan on August 7, 2003 for Isooctadecanoic Acid reaction products with TEPA. The Council proposes to do an OECD 422 Test Protocol, a combined repeat dose/reproductive/developmental screen, which will kill approximately 675 animals, and an OECD 473 Test Protocol, a chromosomal aberration test. We are pleased that ACC has elected to use human lymphocytes for this latter test.

The major uses and human exposure scenarios are briefly described in the test plan, along with general substance information. Isooctadecanoic Acid reaction products with TEPA is acutely non-toxic, with an oral LD50 value of greater than 5 g/kg in the rat, and an acute dermal LD50 value of greater than 2 g/kg in the rabbit. Again, this reaction product, with low acute toxicity, should be considered a low priority chemical for testing under HPV, especially since there are no relevant physical-chemical data available. These latter data should certainly be developed prior to initiating additional animal testing, and it is unfortunate that another 675 animal will be killed to check all boxes in the program.

The fact is that additional animal testing on a substance of this nature and prior to knowing its physical-chemical properties violates principles set forth in both the October 14, 1999, letter to HPV participants and the December 2000 *Federal Register* notice (Wayland, S.H., Oct. 4, *http://www.epa.gov/chemrtk/ceoltr2.htm*; *Federal Register*, "Data collection and development on HPV chemicals," Vol. 65, No. 248, Dec. 26, p. 81691) which specifically state that:

*In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested.*

*As with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant.*

If ACC insists on conducting the OECD 422 for these endpoints, we request that ACC also conduct the rodent embryonic stem cell test (EST) in parallel.

As you are aware, this *in vitro* embryotoxicity test method has been validated by the European Centre for the Validation of Alternative Methods, and the Centre's Scientific Advisory Committee has concluded that this test is ready to be considered for regulatory purposes (Genschow 2002). The animal protection community has urged individual companies to consider the use of this test, and has provided validation and SOP references. We suggest that, in this screening level program, a positive result found in the EST should warrant the substance's treatment as a developmental toxicant/teratogen, and that no further testing should then be carried out.

Several individual companies have expressed interest in running the EST in parallel with the OECD 421/422. Though doing so will not spare any animals' lives in the current context, it does help build a database for industrial chemicals for eventual validation of the EST in the U.S. To its credit, at least one company has agreed to the extra expenditure of funds to run four of its HPV chemicals through the EST. It is also worthy of note that the cost of the test is a fraction of the cost of the 422.

The ACC-- as one of the key players in the development of the HPV program -- has a specific responsibility to help with the validation and incorporation of non-animal test methods. We hope to receive a positive response that the ACC will also run the EST for Isooctadecanoic Acid reaction products with TEPA. We would be happy to provide further information on a local laboratory that conducts this test.

Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 335, or via e-mail at kstoick@pcrm.org.

Sincerely,

Kristie M Stoick, M.P.H.
Research Analyst

Chad B. Sandusky, Ph.D.
Director of Research